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Previous attempts to utilize oral fluid to screen for HCV exposure have been largely unsuccessful, likely due to the vastly decreased levels of antibody present in the oral fluid compared to serum or plasma as well as the inability to detect other classes of anti-HCV than IgG. A method capable of utilizing oral fluid as an alternative to serum or plasma provides many advantages over traditional blood-based analyses. Oral fluid collection is rapid and non-invasive and eliminates the risks of needle exposure. Oral fluid can be collected by non-medical personnel, relieving health care professionals of the time-consuming and economic burden of obtaining serum samples. Furthermore, oral fluid-based assays may prove to be the preferred method of testing for infants, young children and in developing nations, as well as for patient groups where blood collection is difficult, such as intravenous drug users, that constitute a significant portion of total HCV cases.